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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/436,347	11/09/1999	CHRISTINE A. WHITE	012712-643	6491

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EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 04/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/436,347	WHITE ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/18/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Claims 1-27 are pending.

Claims 1, 7, 9, 12, 14 and 17 have been amended.

Claims 19-27 have been added.

Claims 1-27 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

3. The rejection of claims 1-12 and 14-17 under 35 U.S.C. 112, second paragraph, set forth February 29, 2000 as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of Applicants' amendments to the claims.

Claim Rejections - 35 USC § 102

4. The rejection of claims 1, 2, 4, 6-9 and 11-17 under 35 U.S.C. 102(b) as being anticipated by Maloney et al. (Blood 90(6): 2188-2195, 1997) is withdrawn. Abstract. This activity clearly reflects that the MoAb was administered in an amount

5. The rejection of claims 1-4, 7 and 11-17 under 35 U.S.C. 102(a) as being anticipated by Ford and Donegan (Highlights in Oncology Practice 16(2):40-50, 1998) is withdrawn.

Claim Rejections - 35 USC § 103

6. The rejection of claims 1-7 and 9-18 under 35 U.S.C. 103(a) as being unpatentable over Ford and Donegan (Highlights in Oncology Practice 16(2):40-50, 1998) is withdrawn.

7. The rejection of claims 1, 2, 4-9 and 11-18 under 35 U.S.C. 103(a) as being unpatentable over Maloney et al. (Blood 90(6): 2188-2195, 1997) is withdrawn.

8. The rejection of claims 1-4, 7, 8 and 11-17 under 35 U.S.C. 103(a) as being unpatenable over Ford and Donegan (Highlights in Oncology Practice 16(2):40-50, 1998), in view of Hudziak et al. (U.S. Patent # 5,677,171, October 14, 1997) is withdrawn.

9. The rejection of claims 1, 2, 4, 6-9 and 11-17 under 35 U.S.C. 103(a) as being unpatenable over Maloney et al. (Blood 90(6): 2188-2195, 1997), in view of Hudziak et al. (U.S. Patent # 5,677,171, October 14, 1997) is withdrawn.

Maintained Rejections and New Grounds of Rejection

Claim Rejections - 35 USC § 112

10. The rejection of claim 7 under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure without complete evidence either that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological materials is maintained.

Applicants have asserted that the complete sequence of rituximab antibody is listed in U.S. Patent No. 5,736,137 and that the RITUXAN® (rutximab) antibody is publicly available as deposit number 69119 from the American Type Culture Collection. These arguments and points of view have been carefully considered but found unpersuasive.

The Examiner has attempted to verify the deposit number with the RITUXAN® (rituximab) antibody and has not found any evidence that this number (#69119) has been assigned to the said antibody. Furthermore, as the Remarks set forth within the bridging sentence on pages 8 and 9 patent '137 that only the light and heavy chains of the variable regions are disclosed. Remiss from the disclosure is information revealing the hinge region and constant regions (light and heavy). As set forth in preceding Office Actions there needs to be assurance in the instant case that the deposit is made under the provisions of the Budapest Treaty and that the deposits comply with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits. Such

assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record that has the authority.

11. Claims 1-12 and14-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **THIS IS A NEW MATTER REJECTION.**

Applicants have amended claims 1, 12, 14 and added new claims 19-27 to include recitations such as "at least about 40 x 10^9 white blood cells per liter", "in the range of about 40 x 10^9 cells per liter to about 200 x 10^9 cells per liter" and "in the range of about 98 x 10^9 cells per liter to about 200 x 10^9 cells per liter". Applicants assert that these recitations, particularity the recitation noting "40 x 10^9 white blood cells per liter" is found within the specification at pages 12 and 13, the bridging sentence. What is clear from this sentence is *the medium white blood cell count was 40 x 10^9* per liter and that the range encompassed 4-200. The specification does not provide support that Applicants have contemplated that the malignancy has *at least* 40 x 10^9 white blood cells per liter. It is not clear how Applicants established the claimed range. Applicants are advised to delete the new matter or explicitly make of record the page and line numbers where in the specification support is found for newly added claim language.

12. Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 7 is vague and indefinite in the recitation "RITUXAN® (rituximab)" because it is not clear if Applicants are addressing just the monoclonal antibody or the said antibody with additional products.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

14. Claims 1-4 and 7-27 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent number 6,455,043 (effective filing date August 11, 1998). U.S. Patent

#6,455,043 discloses a method of treating patients with a variety of B-cell lymphomas, including chronic lymphocytic leukemia (CLL) and high grade lymphoblastic non-Hodgkin's lymphoma with an anti-CD20 antibody, see Abstract and column 2, line 1-column 4, line 54. The anti-CD20 antibody could be chimeric, humanized, radiolabeled and preferentially is C2B8 (IDEC Pharmaceuticals, rituximab), see column 2, line 54-column 3, line 3. CLL patients with a medium white blood cell count of 40 x 10^9 per liter were treated and the range varied between 4-200, see column 10, line 59-column 11, line 5. The anti-CD20 antibody administration could be implemented as a combined therapy inclusive of cytokines and chemotherapy, see column 3, lines 23-47; column 11, lines 56-59; column 13, line 19-column 16, line 11. With the administration of a lymphokines such as GM-CSF and TNF-alpha there was upregulation of CD20, see column 11, lines 20-25, 31-36; column 15, lines 43-63.

The patent discloses several means of performing the disclosed methodology at varying dosages and times of dispensing. For instance, rituximab was infused at 375 mg/m^2 weekly times four, see column 9, lines 1-6; column 10, lines 43-46; a dose escalation of rituximab was administered at dose of 125, 250, or 375 mg/m^2 weekly X4, see column 13, lines 55 and 56. There was a reduction in peripheral blood lymphocystosis, which renders a reduction in circulating tumor cells, see column 11, lines 12-15. The useful disclosed method "...will be particularly useful for patients who are refractory...after treatment with chemotherapeutic drugs.", see column 12, lines 1-3.

Furthermore, with the administration of the disclosed antibody inherently implemented is a method of avoiding or reducing the toxicity associated with the disclosed ranges would be implemented.

Claim Rejections - 35 USC § 103

15. Claims 1-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent number 6,455,043 (effective filing date August 11, 1998). The patent does not teach the administration of the antibody at a dosage ranging from 0.1 to 30 mg/kg weekly for about 2 to 10 weeks.

However, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to administer the anti-CD20 antibody in the recited dosages at the designated time points. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings well known in the art, that the dosages of any therapeutic agent must be adjusted and optimized. Additionally, the patent provides the impetus for one of ordinary skill in the art to optimize and implement varying dosages in order to identify a useful treatment regimen because in several instances within patent '043 suggest several administration plans, see column 13, lines 14-17, lines 31-33, lines 52-58.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is

(571) 272-0831. The examiner works a flexible schedule, however can normally be reached between the hours of 7:00 am to 4:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne "Bonnie" Eyler, Ph.D. can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
15 April 2004